REMARKS

Claims 170-172, 176-178, 188-193, and 195-197 were pending in the application. Of these, Claims 170-172, 188, 190, 192 and 196 were examined, while Claims 176-178, 189, 191, 193, 195 and 197 were withdrawn from consideration. By virtue of the instant Response, Applicants hereby amend Claims 170, 191 and 192, and cancel Claims 176-178, 189, 190, 193 and 195-197. Thus Claims 170-172, 188, 191 and 192 are currently pending.

I. Claim Rejections - 35 USC § 112

Claims 170-172, 188, 190, 192, and 196 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, allegedly fails to provide enablement commensurate with their scope. In particular, the Examiner states that "the specification, while being enabling for the claimed methods wherein the core particles is one of the core particles identified as being capable of assembly in Table 15 of the application, does not reasonably provide enablement for the claimed methods of use for any rodent hepadnaviral core protein particle as claimed for the production of an immune response against any antigen" (Office Action, page 2). Applicants respectfully traverse this rejection and its supporting remarks.

Nonetheless, Applicants hereby amend Claims 170, 191 and 192, and cancel Claims 176-178, 189, 190, 193 and 195-197, in order to further the prosecution of the present application and Applicants' business interest, without acquiescing to the Examiner's arguments, while preserving the right to prosecute the original, similar or broader claims in one or more future application(s). In particular, Applicants hereby amend Claim 170 to recite "a hybrid particle comprising a fusion protein comprising a rodent hepadnavirus core antigen and a heterologous antigen, wherein said hybrid particle is a hybrid ground squirrel hepadnavirus particle that assembles satisfactorily of Table 15, or woodchuck hepadnavirus particle that assembles satisfactorily of Table 11, Table 12, Table 13, Table 15, or Table 16." Support for this amendment can be found but is not limited to the recited tables and Examples 8-10, which describe the hybrid woodchuck and ground squirrel hepadnavirus particles that were produced prior to the filing date of

the instant application. Further support can be found in the description of rapid screening technology, which teaches that a

> strong correlation between the relative lysate assembly scores and the ability to purify hybrid core particles in high yield has been observed during development of the present invention. Every hybrid particle construct with an assembly score of three or greater in the transformed bacterial lysate has yielded easily-purifiable particles (US 2008/0131452, paragraph [0231]).

Thus, the amended claims encompass methods of producing an immune response by administration of a hybrid rodent particles actually produced during development of the present disclosure. This includes hybrid rodent particles with an assembly score of 3 or greater of Table 11, hybrid rodent particles described as assembling satisfactorily of Tables 12 and 13, hybrid rodent particles with a positive (+) assembly score of Table 15, and the purifiable hybrid rodent particles of Table 16 (e.g., > 2 mg/L).

Since the amended claims are directed to methods of producing an immune response to hybrid rodent particles actually produced during development of the present disclosure, the amended claims are clearly enabled. Accordingly, Applicants respectfully request that this rejection be withdrawn.

II. Claim Rejections - 35 USC § 103

Claims 170-172, 188, 190, 192, and 196 stand rejected under 35 U.S.C. 103, as allegedly unpatentable over Birkett (US 2003/0054337) in view of Paoletti, Maruyama, and Shodel. Applicants respectfully traverse this rejection and its supporting remarks.

Nonetheless as described above in Section I, Applicants have amended the claims to read upon the species of Tables 11, 12, 13, 15 and 16. The hybrid rodent particles of the pending claims, differ from the hybrid human particles of Bikett, not only in terms of a rodent versus HBV core antigen sequence, but also in terms of one or more of epitope, insertion site, and C-terminus. Only the NANPNVDP$(NANP)_3$ epitope of SEQ ID NO:3 of Birkett corresponds to an epitope of an embodiment of Applicants' hybrid rodent particles (e.g., M epitope of SEQ ID NO:75). The

heterologous antigen of Birkett's hybrid HBV particles of pages 26 and 27 were all inserted at position 78 of the HBV immunodominant loop (LEDPAS) (Birkett, paragraph [0266]). However as shown in the alignment in Figure 46B, there is zero percent identity with the immunodominant loops of both ground squirrel (TT-EEV) and wood chuck (ITSEQV) hepadnavirus core antigens. Moreover, there is a deletion of the residue corresponding to D^{78} in the ground squirrel core. Additionally, the C-terminus of the HBV cores of Birkett contained a *P. falciparum* universal T cell epitope bounded to position V^{149}. In contrast, none of the hybrid rodent cores of the pending claims possessed a malarial C-terminus in place of the native hepadnavirus C-terminus.

The other three references cited by the Examiner, do not remedy these deficiencies, since only Birkett actually teaches the production of a fusion protein, albeit a fusion protein comprising an HBV core. These noteworthy structural differences in combination with Applicants disclosure that both the insert site and C-terminal sequence influence hybrid particle expression and assembly, indicate that the pending claims are not obvious over the cited references. Accordingly, Applicants respectfully request that this rejection be withdrawn.

III. Double Patenting

A. Claims 170-172, 188, 190, 192 and 196 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over Claims 31-44 of co-pending Application No. 11/635,271. Applicants respectfully disagree with this rejection. However, abandonment of the '271 Application has rendered this rejection moot.

B. Claims 170-172, 188, 190, 192 and 196 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over Claims 31-88 of co-pending Application No. 11/635,275. Applicants respectfully disagree with this rejection. However, in the interest of advancing prosecution in this case, enclosed herewith is a terminal disclaimer over the '275 Application.

C. Claims 170-172, 188, 190, 192 and 196 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over Claims 32, 36-44

and 47-64 of co-pending Application No. 12/008,059. Applicants respectfully disagree with this rejection. Nonetheless, a terminal disclaimer over '059 Application was already provided to the Office on August 26, 2009, and approved by the Office on September 24, 2009. Accordingly this rejection has already been fully addressed.

IV. Conclusion

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. **643802000203**. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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